Participant Information Sheet and Informed Consent Form

Protocol Title:	A Randomized, Double-Blind, Placebo-Controlled Study to Evaluate the Efficacy and Safety of SPR001 (Tildacerfont) in Reducing Supraphysiologic Glucocorticoid Use in Adult Subjects with Classic Congenital Adrenal Hyperplasia
Protocol No.:	SPR001-204
EU CT No.:	2023-503771-13 [*for E.E.A. countries only*]
Sponsor:	Spruce Biosciences, Inc. 611 Gateway Blvd, Suite 740 South San Francisco, CA 94080, USA
Study Doctor:	[Insert Principal Investigator name and address]
24-hr. Telephone #:	[Insert 24-h phone number]

For E.E.A. countries only

Data Protection Officer:	[Insert DPO name and e-mail address] **Sponsor's Data Protection Officer:** The DPO Centre 50 Liverpool Street London, EC2M 7PY, UK advice@dpocentre.com

If Sponsor is located outside E.E.A.

Data Representative:	[Insert data representative name and e-mail address if sponsor is outside EU]

Introduction

You are being invited to take part in a research study. Before agreeing to participate in this research study, it is important that you read and understand why this research is being done and what it will involve for you. This participant information and informed consent form describes the purpose, procedures, benefits, risks, discomforts, and precautions of the study. It also describes the alternative treatments that are available to you and your right to withdraw from the study at any time.

The study doctor or a member of the study staff will go through this participant information and informed consent form with you and explain the study to you. Please read the following information carefully and ask any questions you may have. Please discuss taking part with your family, friends, and your personal doctor/General Practitioner (GP), if you wish. You can take as much time as you would like to make your decision.

Background and Purpose

You are being asked to participate in this research study because you have congenital adrenal hyperplasia (CAH). CAH is an inherited genetic disorder that affects the adrenal glands, a pair of walnut-sized organs above your kidneys. The disease affects the production of steroid hormones by the adrenal glands, which include “glucocorticoids” such as cortisol, which regulate your body’s response to illness or stress.

The adrenal glands also control the production of androgens (sex hormones). People with CAH often have abnormal levels of certain adrenal sex hormones, which can have negative effects on overall health.

The current standard of care for CAH is the use of glucocorticoids (GCs). These can have significant side effects and do not always work well in treating CAH. A non-steroidal treatment option that helps control adrenal hormone levels when used with GCs may benefit CAH patients.

This study involves the use of an investigational drug, tildacerfont (SPR001). Investigational means that the study drug has not been approved by the United States Food and Drug Administration (FDA), European Medicines Agency (EMA), or other regulatory agencies for use as a prescription or over-the-counter medicine. The purpose of this study is to see if tildacerfont can change overall amount of GC (e.g., hydrocortisone) you need to take while you in the study.

Because this is a scientific study, it is also important to collect information about patients with CAH who are not receiving tildacerfont. Therefore, tildacerfont will be compared to “placebo”, which is a medication that looks like the investigational drug but does not contain any tildacerfont or any other active compound. Throughout this form, both tildacerfont and placebo are referred to as “study drug”.

Voluntary Participation/Withdrawal

Taking part in this research study is voluntary and entirely up to you. You will have to sign and date the consent page within this participant information and informed consent form to indicate you choose to take part. You will be provided with a copy of each signed consent form. You may change your mind and withdraw without giving any reason, at any time. If you choose to not participate or you withdraw from the study, you will not lose any medical benefits to which you are entitled, and it will not have any effect on your future medical care.

You may decide to stop taking part in the study by notifying the study doctor of your decision. If you have some unresolved health problems when you leave the study, the study doctor may, if you agree, need to collect information about your health until the problem resolves.

If you choose to withdraw before the planned final visit, you will be asked to complete as many of the originally intended study visits as you are willing to complete. If you are unable to complete the remaining study visits, you will be asked to come back to the study clinic to have some procedures done so that you can leave the study safely.

Alternative Treatment

You do not need to take part in this study to get treatment for your CAH.

The current standard of care for CAH is treatment with GCs to replace cortisol, often at doses that are much higher than those normally found in the body. In addition, mineralocorticoids (such as fludrocortisone) may be used to replace aldosterone. The study doctor will discuss with you the risks and benefits of the alternative treatments. You should discuss your alternatives to participating in this research with the study doctor or study staff. In addition, you may discuss your options with your regular health care provider.

Number of Participants/Length of Participation

Approximately 90 participants will participate in this study at approximately 130 study sites globally.

Your participation in this study will last up to approximately 84 weeks and will include up to 16 study visits to the clinic and 5 telephone calls.

Study Visits

You should make every effort to attend the clinic for all study visits as per study doctor judgement or your preference. If you are unable to accommodate a clinic visit (for example, due to restrictions from the COVID-19 pandemic, or other logistical challenges), some of the tests and procedures may be performed by a healthcare professional at your home (called a home health visit), as long as your home can accommodate such a visit.

If it is determined that a home health visit is needed, a qualified medical professional, provided by the home health care provider, will contact you to schedule the home visit. The study staff will discuss with you the importance of scheduling these visits well in advance so that a nurse can be prepared for your home health visit. The home care nurses supporting this study will be trained on this study and will communicate with the study doctor and the study staff. In order to conduct the home visits, the home care nurse and the home care services provider will have access to your personal data including individually identifiable protected health information, such as your name, address, and phone number. The home care services provider may also have access to your personal medical information as needed to schedule and conduct the home health visits.

Please refer to the confidentiality section of this consent for more information around the use of your personal data and discuss any questions you may have with the study doctor/study staff. Please also speak to the study doctor and study staff about any questions regarding the home health care services and how these visits will be carried out, if needed.

Participant Responsibilities

If you are to participate in this study and the study doctor allows you to enroll in the study, you will have the following responsibilities:

- Do not take part in any other medical research studies;
- Give correct and accurate information about your medical history and current medical condition;
- Follow the study staff's directions about the study;
- Take your GC and study drug dose as instructed by the study doctor;
- Complete your electronic diary (eDiary) for study drug and GC taken according to the study staff's instructions;
    - If you are female, enter your menstrual information (if applicable) in your eDiary according to the study staff's instructions;
- Attend all scheduled study visits and complete the study tests and procedures. Prior to some of your study visits, you will be required to fast (no food and nothing to drink except water after midnight);
- Carry your Patient Emergency Card with you at all times while participating in this study;
- Talk to the study doctor before taking any new medication during the study. While you are taking the study drug, there are some other medications that you should not take as they may interfere with the study drug and it may be unsafe for you to take them together. The study doctor will tell you what other medications you can take while you are on the study drug;
- Tell the study doctor about any side effects or problems that you experience during the study;

- Follow birth control requirements;
- Do not become pregnant or cause your partner to become pregnant;
- Do not donate blood or blood products, sperm or eggs, as described in the ***Pregnancy Risks*** section below;
- Do not eat grapefruit or drink grapefruit juice during your participation in the study;
- Do not participate in heavy exercise for 8 hours before any visit where blood samples will be drawn;
- Do not participate in any type of exercise within 30 minutes before any study procedure.

Study Design

This study will consist of four periods:

Screening: This period will last approximately 30-45 days. If you decide to take part in the study, you will be asked to sign the informed consent form before any study related tests or procedures can be done. During the Screening period, you will be asked questions and have certain tests and procedures done to see if you can continue in the study.

If the study doctor determines that you are eligible for the study after Screening, you will enter either the Glucocorticoid Conversion period or the Treatment period. If you are taking dexamethasone at Screening, you will enter the Glucocorticoid Conversion period. If you are not taking dexamethasone at Screening, you will not need to enter the Glucocorticoid Conversion period after Screening and you will enter directly into the Treatment period.

Glucocorticoid Conversion: This period will last 6 or 12 weeks. During this period, you will stop taking dexamethasone and will switch to a new GC regimen, which will be determined by the study doctor. You will also have additional tests and procedures during this period to determine if you can move on to the Treatment period. You will not yet begin to take any tildacerfont or placebo during the Glucocorticoid Conversion period.

Treatment: If the study doctor determines that you continue to be eligible for the study following either the Screening period or the Glucocorticoid Conversion period, you will enter the Treatment period, which will last 76 weeks. The Treatment period will consist of a 24-week double-blind phase and a 52-week open-label phase.

- **Double-blind Phase:** You will be randomly assigned by chance (like the flip of a coin) to receive either tildacerfont or placebo during the double-blind phase of the study. You will have a 50% (1 in 2) chance of receiving tildacerfont and a 50% (1 in 2) chance of receiving placebo. Double-blind means that neither you nor the study doctor will know which study drug (placebo or tildacerfont) you are taking. This is done so that a fair evaluation of the results can be made.
- **Open-label Phase:** Once the double-blind phase is complete, you will enter the 52-week open-label phase, and you will receive tildacerfont with no possibility of receiving placebo. Open-label means that you and the study doctor will know that you are taking tildacerfont.

During the Treatment period, the study doctor may adjust your GC dose per the study requirements, based on test results at each visit and your symptoms. Specifically, your GC dose may be decreased, increased, or kept at the same dose level after each visit over the course of the Treatment period, and the time you take your GC dose may be adjusted.

During the Glucocorticoid Conversion period and the Treatment period, you will have the option to receive your GC supply and study drug assignment at home or your place of work (or location that is convenient for you), if you agree and locally approved, unless you indicate to the study doctor that you would like to receive it at the study clinic, which will require an additional visit to pick up your medication. Direct to Patient (DTP) shipments enables medication to be delivered to you at a location and time that is convenient for you. The courier

company (*update per country* [US: Marken, FedEx, or other equivalent courier; EU: Marken, DHL, or other equivalent courier; Australia: Marken or other equivalent courier]) will be provided your contact details (name, email, and telephone number, and name if any of your authorized representative) in order to contact you and understand where and when the medication could be delivered, as long as this is within the required protocol timings window. The courier will then use your delivery details to identify a qualified driver who will deliver the medication at the required time and location to you. Upon delivery of the medication, you may be asked by the driver to provide identification to confirm your identity, sign for receipt, unpack the medication and hand over the packaging to the driver. Please ask the study doctor if you would like additional information on the courier company that will be used.

Follow-up: This period will last 30 days after your last dose of the study drug. During this period, follow-up safety tests and procedures will be performed, and you will continue your GC dosing regimen and recording in your eDiary. After completion of the study, your GC dosing regimen will be managed outside of the study by your regular physician.

Because this is a clinical research study, the study drug will be given to you only during this study and not after the study is over. However, after you complete all of the Treatment Period study visits, and based on the study results, you may be able to continue to receive tildacerfont in an optional open-label extension period for an additional 240 weeks/5 years. You will need to sign a new participant information and informed consent form to participate in the open-label extension period.

Procedures

Screening

If you provide your consent to participate by signing this informed consent form, you will come to the clinic for the following screening tests and procedures to see if you can continue in the study:

- Information will be recorded about you, including date of birth, gender, ethnic origins, race (demographic data);
- You will be asked questions about your past and present health including clinically significant family history (a medical history);
- You will be asked about any medicines you are currently taking or have taken recently, which may include any non-prescription medicines, food supplements, and natural remedies;
- You will have a physical examination, which will include measuring your weight, height, and waist circumference;
- Your blood pressure, heart rate, temperature and breathing rate will be measured;
- You will be asked questions to assess your symptoms and find out how your CAH is affecting your quality of life;
- The study staff will provide instructions on how to complete your eDiary;
- Blood samples will be collected from you. You will be required to fast (no food and nothing to drink except water after midnight) before this visit. On the morning of the visit, **you will be required to wait to take any morning GC dose until after your lab tests are completed.** If these requirements are not met, your visit will need to be rescheduled. About 50 mL (10 teaspoons) of blood will be collected from you for the items noted below:
    - To perform a standard safety laboratory panel to assess your health, including the function of your kidney, liver, and other important organs, and the amount and type of cells in your blood;
    - To measure hormone levels in your blood;
        - If you did not participate in the optional pre-screening for this study, about 10 mL (2 teaspoons) of additional blood will be collected during this visit;

        - To assess metabolic parameters, including levels of Hb1Ac;
        - To test if you are pregnant, if you are a female of child-bearing potential;
        - To test for hepatitis B and C and human immunodeficiency virus (HIV). You cannot take part in this study if you have any of these infections. *If applicable for the country:* [hepatitis B and C/HIV] are notifiable diseases in [country name]. This means that if you test positive for hepatitis B and C, and/or HIV, your test results will be reported to [name of country health authority];
- A urine sample will be collected from you:
    - To perform a drug screen;
    - To assess your health;
- You will have a 12-Lead electrocardiogram (ECG) – a recording of the electrical activity in your heart.

If applicable, your screening information from another Spruce Biosciences study with tildacerfont (SPR001-203) may be used to determine eligibility and fulfill screening assessments for this study.

Washout

Certain medications are not allowed to be taken during this study. If you are taking any of these medications, the study doctor may determine whether or not it is safe for you to stop taking the medication and wait for a period of time for the medication to leave your body. If it is safe, you will be able to rescreen after that period of time. This is called a washout period, during which the effects of the medication leave your body.

Glucocorticoid Conversion

If the study doctor determines that your results from the Screening period allow you to continue in the study, you will enter the Glucocorticoid Conversion period, only if you are taking dexamethasone at Screening. The following tests and procedures will be performed during this period. Not all of these procedures will be performed at each visit. Please refer to the table below for when each procedure will take place:

- You will take your GC dose and record in your eDiary;
- You will be contacted by telephone by the study staff to discuss your GC dosing regimen and overall health;
- You will be asked about how you have been feeling since your last visit;
- You will be asked about any medicines you are currently taking or have taken recently;
- You will have a physical examination;
- The study staff will review your eDiary;
- Blood samples will be collected from you. You will be required to fast (no food and nothing to drink except water after midnight) before this visit. On the morning of the visit, **you will be required to wait to take any morning GC dose until after your lab tests are completed.** If these requirements are not met, your visit will need to be rescheduled. About 30-33 mL (6-6.5 teaspoons) of blood, depending on the visit, will be collected from you at each visit for the items noted below:
    - To perform a standard safety laboratory panel to assess your health;
    - To measure hormones levels in your blood;
- If you are a female of child-bearing potential, a pregnancy test will be performed using a urine sample;
- Your body weight, blood pressure, heart rate, temperature and breathing rate will be measured.

During this period and the Treatment period, the study drug may be shipped to your home or place of work (or location that is convenient for you) directly or picked up at the study clinic. You may need to identify a representative(s) to receive this study drug delivery if you are not always going to be available. The study coordinator will record who those people are, and their

information will be maintained by the company (*update per country* [US: Marken, FedEx, or other equivalent courier; EU: Marken, DHL, or other equivalent courier; Australia: Marken or other equivalent courier]) who will deliver the material to your home or location that is convenient for you. That information is maintained in accordance with country specific data protection and privacy requirements. By signing this document, you:

- Agree to have the study drug delivered to your home (or work or other specified location) unless you indicate to the study doctor that you want to receive it at the clinic.
- You accept that the courier company will have your name, address (or address of specified location) and telephone number. This information will be handled with strict confidentiality. The Sponsor of the study will not receive this information under any circumstances.
- Your information will be kept by the courier for 7 years from the end of the study. This period is based on authority directives. After the 7 years, your information will be permanently deleted from the courier's records.

Treatment Period

If the study doctor determines you are able to continue in the study, you will enter the Treatment period. During this period, you will take the study drug with an evening meal every night, which should be eaten between 6 pm and midnight. The evening meal should contain approximately 25-50% fat content.

You will continue to take the Sponsor-provided GC medication during this period. The Sponsor of the study, Spruce Biosciences, will be able to provide support with transportation and/or overnight stays close to the clinic, if needed. This support will be provided through a separate company who will coordinate with the study staff to help your logistic needs.

The following tests and procedures will be performed during Treatment period. Not all of these procedures will be performed at each visit. Please refer to the table at the end of this section for when each procedure will take place:

- You will receive the study drug at the study clinic to take at home or it will be shipped directly to your home;
- You will record each dose of study drug in your eDiary. This includes the time and whether the dose was taken with food;
- You will record each dose of GC that you take in your eDiary;
- You may be contacted by telephone by the study staff to discuss your GC dosing regimen;
- You will be asked about any medicines you are currently taking or have taken recently;
- You will be asked about how you have been feeling since your last visit;
- The study staff will review your eDiary;
- You will have a physical examination;
- You will have a dual energy X-ray absorptiometry (DXA) scan of your whole body. A DXA scan measures total body composition (mass of fat, bones and lean tissue) and the strength of your bones;
- If you are a male, you will have a scrotal ultrasound to check for and measure the size and number of any potential testicular adrenal rest tumors (TARTs). An ultrasound is an imaging method that is used to make pictures of organs inside your body;
- You will be asked questions regarding your CAH and your mental health;
- Blood samples will be collected from you. You will be required to fast (no food and nothing to drink except water after midnight) before this visit. On the morning of the visit, **you will be required to wait to take any morning GC dose until after your lab tests are completed.** If these requirements are not met, your visit will need to be

rescheduled. About 26-52 mL (5-10.5 teaspoons) of blood, depending on the visit, will be collected from you at each visit:
    - To perform a standard safety laboratory panel to assess your health;
    - To measure hormone levels in your blood;
    - To assess metabolic parameters, including fasting glucose levels, fasting insulin levels and levels of Hb1Ac;
    - To measure levels of bone turnover;
    - To measure how your body absorbs, distributes, and gets rid of the study drug (pharmacokinetics or PK);
    - To assess genes related to your CAH as well as genes related to how the study drug acts on your body. The blood sample for genetic testing will only be collected at Visit 5 and is completely voluntary. Your sample may also be stored for future genetic testing. Please indicate whether you would like to provide a sample for genetic testing in the Genetic Testing section of the consent form;
- Your body weight and waist circumference will be measured;
- Your blood pressure, heart rate, temperature and breathing rate will be measured;
- A urine sample will be collected from you to assess your health;
- If you are a female of child-bearing potential, a pregnancy test will be performed using a urine sample;
- You will have a 12-Lead ECG to measure your heart function;
- You will be asked to complete questionnaires about your quality of life and the status of your CAH and overall health.

Follow-Up

Following your last study visit in the Treatment period, you will either continue to receive tildacerfont in the optional open-label extension period or you will enter the Follow-up period. The study doctor will discuss your options with you. If you enter the Follow-up period, this period will occur 30 days after your last dose of study drug. During the Follow-up period, the following tests and procedures will be performed:

- You will be asked about any medicines you are currently taking or have taken recently;
- You will continue your GC dosing regimen and recording in your eDiary;
- The study staff will review your eDiary;
- Your GC dosing regimen will be assessed;
- You will have a physical examination;
- You will be asked about how you have been feeling since your last visit;
- Blood samples will be collected from you. You will be required to fast (no food and nothing to drink except water after midnight) before this visit. On the morning of the visit, **you will be required to wait to take any morning GC dose until after your lab tests are completed.** If these requirements are not met, your visit will need to be rescheduled. About 47 mL (9.5 teaspoons) of blood will be collected from you:
    - To perform a standard safety laboratory panel to assess your health;
    - To measure hormone levels in your blood;
    - To measure levels of bone turnover;
    - To measure how your body absorbs, distributes, and gets rid of the study drug (pharmacokinetics or PK);
- Your body weight, blood pressure, heart rate, temperature and breathing rate will be measured;
- If you are a female of child-bearing potential, a pregnancy test will be performed using a urine sample;
- You will have a 12-Lead ECG to measure your heart function.

Early Termination (ET) Visit

If your treatment with the study drug stops early and you don't wish to continue with the study visits, you will have an Early Termination (ET) visit. Assessments that would be done at the follow-up visit will be done at the ET visit along with the following:

- A urine sample will be collected to assess your health;
- You will be asked to complete questionnaires about your quality of life and the status of your CAH and overall health;
- Your waist circumference will be measured;
- If you are a male, you may be required to have a scrotal ultrasound;
- You may have a DXA scan of your whole body;
- The study staff will review your eDiary;
- You will be asked about how you have been feeling since your last visit.

Please see below table for when each procedure described above will be performed:

	Screening Period	Glucocorticoid Conversion Period						Treatment Period													Follow-up	ET
								Double-blind Treatment Phase						Open-Label Phase								
Study Visit Number	**1**	**2**		**3**			**4**	**5**	**6**	**7**	**8**	**9**	**10**		**11**	**12**		**13**	**14**	**15**	**16**	
Study Week		**-12**	**-11**	**-8**	**-6**	**-5**	**-2**	**0**	**3**	**6**	**12**	**18**	**24**	**27**	**32**	**40**	**46**	**52**	**64**	**76[2]**	**80**	
Visit (V) / Telephone Contact (T)	**V**	**V**	**T**	**V**	**T**	**T**	**V**	**V**	**V**	**V**	**V**	**V**	**V**	**T**	**V**	**V**	**T**	**V**	**V**	**V**	**V**	**V**
Informed consent	X																					
Demography	X																					
Review of your medical history	X																					
Hepatitis B & C and HIV screening	X																					
Review of your medications	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X
Pregnancy test	X	X						X		X	X	X	X		X	X		X	X	X	X	X
Physical exam	X	X		X			X	X		X	X	X	X		X	X		X	X	X	X	X
12-Lead ECG	X							X			X		X					X		X	X	X
Vital signs and body weight	X	X		X			X	X	X	X	X	X	X		X	X		X	X	X	X	X
Height	X																					
Waist circumference	X							X					X					X		X		X
Questionnaires about your quality of life and CAH	X							X			X		X					X		X		X
Urine sample for drug test	X																					
Blood sample for safety evaluation	X	X		X			X	X	X	X	X	X	X		X	X		X	X	X	X	X
Urine sample for safety evaluation	X							X					X					X		X		X
Blood sample for research purposes	X	X		X			X	X	X	X	X		X					X		X	X	X
Blood sample for genetic testing								X														
Study doctor assessment of GC dosing regimen [1]	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X
Review how you are feeling		X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X
DXA scan								X					X					X		X		X
Scrotal ultrasound (if applicable)								X					X							X		X
Receive study drug to take home								X		X	X	X	X		X	X		X	X			
eDiary completion/review		◄																				►

1. *If you are eligible for GC dosing regimen adjustments, the study staff will contact you via telephone within 2 weeks following each study visit. If your GC dosing regimen was adjusted during a study visit, the study staff will contact you via telephone within 7 days following your visit to review any changes to the medicines you are taking and ask how you are feeling.*

2. *If you decide to continue in the optional Open-Label Extesion Period, Week 76 visit will be considered as Study Visit number 1 for optional Open-Label Extension Period.*

Genetic Testing

This study may involve genetic testing. DNA is the substance in the cells that make up your genes. Genes are inherited from your parents and carry instructions for the body to grow and develop. This genetic information serves as the “instruction book” for the cells that make up our bodies and helps determine the characteristics of people (such as eye color).

Researchers study genes in order to understand why some people have certain conditions, such as CAH, and why some people do not. Understanding a person’s genes may be able to explain why some people respond to a treatment while others do not, or why some people experience an adverse effect from a medicine and others do not.

If you agree, your blood sample collected at Visit 5 will be used to assess genes related CAH and genes related to how the study drug acts on your body. Your samples may be stored for future testing as described below.

Please indicate below (by signing your initials) whether you agree to have genetic testing performed on your samples and allow your samples to be stored for future genetic testing. You may take part in this study whether you say yes or no to the genetic testing part of this study.

_____ Yes, I allow the Sponsor to perform genetic testing on my blood sample and store any remaining sample for future genetic testing.

_____ No, I do not allow the Sponsor to perform genetic testing on my blood sample and store any remaining sample for future genetic testing.

Biological Samples

The study involves collection of biological samples, such as your blood and urine. Throughout the course of the study, the total amount of blood taken will be approximately 687-697 mL (139-141 teaspoons). Additional blood for lab tests may be collected at the discretion of the study doctor.

For comparison, a standard blood donation at a blood collection center is about 475 mL of blood (about 96 teaspoons/2 cups).

Your samples for the study will be shipped to *(insert Central Laboratory and Specialty Laboratory)* and stored for analysis. *If applicable list all the laboratories in the Master ICF.* Blood samples collected during this study will be stored for future use for biomarker testing, genetic testing or additional testing related to CAH. The samples will be stored on behalf of the Sponsor for up to 5 years after the last study visit of the last patient in the study.

If you withdraw from the study, you can ask the study doctor *update per country regulations* [in writing] for your [identifiable] samples to be destroyed at any time. However, data already obtained from your samples will continue to be kept and used for the purpose described in this participant information and informed consent form.

Stress GC Dosing

As a person with CAH, you will be already familiar with the need to occasionally “stress dose” with GCs, most likely hydrocortisone, due to illnesses or stressors that occur which are impactful to CAH patients. During this study, if you experience symptoms that would make you wish to stress dose as part of your overall self-management of the disease, please inform the study doctor or a member of the study staff immediately. Hydrocortisone to support stress dosing in response to disease symptoms will be provided by the Sponsor, Spruce Biosciences, during the study. You will be asked to record use of the stress dose medication in the study diary.

Potential Risks, Adverse Effects, Discomforts

Any research has some risks, which may include things that could make you feel unwell, uncomfortable, or could harm you. You might have adverse effects related to the study drug while

taking part in the study. Everyone taking part in the study will be watched for any adverse effects; however, the study team does not know all the effects that the study drug may have on you. These effects maybe mild or serious. In some cases, these effects might be long lasting, or permanent, and may even be life-threatening. The study doctor or study staff may give you medicines to help reduce any adverse effects.

The adverse effects that are most likely to happen to you if you take part in this study are listed below.

Risks Associated with Tildacerfont

Because tildacerfont is investigational, all of its possible adverse effects may not be known. There may be rare and unknown adverse effects. Some of these may be life threatening. You must tell the study doctor or study staff about all adverse effects that you have. If you are not honest about your adverse effects, it may not be safe for you to be in the study.

So far, tildacerfont has been given to 145 healthy volunteers in 5 research studies and 26 CAH patients in 2 research studies. Three additional studies are ongoing (one in healthy volunteers and two in CAH patients). The following adverse effects were reported from both healthy participants and CAH participants:

Very common (may affect more than 1 in 10 people):

- Headache (11.4%)

Common (may affect up to 1 in 10 people, ≥ 2.0%):

- Cough (4.3%)
- Diarrhea (3.8%)
- Back pain (3.8%)
- Upper Respiratory tract infection (2.4%)

Elevation of liver enzymes has been observed with tildacerfont use at doses higher than those administered in this study, which may or may not be associated with pruritis or rash. Your liver function will be monitored throughout the study as part of the laboratory tests, and the study doctor may advise you to stop taking tildacerfont if your liver function is of concern at any time during the study. Restart of tildacerfont dosing is possible, if the study doctor and Sponsor approve.

Tildacerfont is a drug that may act on the central nervous system (CNS). Drugs that act on the CNS may have an effect on your mood. Although the study drug has not been shown to be associated with an increased risk of suicidal thinking or behavior in previous clinical trials, it cannot yet be ruled out that there is an increased risk of suicidality in people who take tildacerfont. Suicidal behavior and thoughts will be monitored throughout the study. If you have any suicidal thoughts during the study, please inform the study doctor immediately.

Other Risks

All medicines have the potential risk of an allergic reaction, which if not treated promptly, could become life-threatening. You should seek medical help right away if you think you have any of the following symptoms of a serious allergic reaction: trouble breathing, or swelling of the face, mouth, lips, gums, tongue, or neck. Other symptoms of an allergic reaction may include rash, hives, or blisters.

It is important that you tell the study doctor about any changes to your health as soon as they occur, whether or not you think they are caused by the study drug.

Ask the study doctor if you have questions about the signs or symptoms of any side effects that you read about in this consent form.

If you experience any unwanted effects, make a note of them and report them to the study doctor at your next scheduled visit. Please tell the study doctor if you have any problems with your health or the way you feel during the study, whether or not you think these problems are related to the study drug. **Please inform the study doctor immediately of any serious unwanted effects.**

Placebo Risk

Some participants in this study will receive a placebo. Taking a placebo is the same as not taking any active medicine. If you receive placebo, your CAH may get worse, stay the same, or improve, just as it may have done without any changes to your current treatment. During the study, your GC medicine will be continued, so you will still be getting standard CAH treatment along with the placebo.

Risks Associated with Study Procedures

Glucocorticoid Conversion and Adjustment

If you are taking dexamethasone at Screening, you will stop taking dexamethasone and will switch to a new GC regimen. If this happens, the GC regimen will be prescribed by the study doctor, and any cost not covered by your insurance will be reimbursed by the Sponsor of the study, during the Glucocorticoid Conversion period. The purpose of switching to a Sponsor-provided GC regimen is to achieve standardization of background GC therapies so that the effects of the study drug can be measured more accurately and consistently. Although the new GC regimen should be comparable to your prior GC regimen, as with any change in medication, you may experience unwanted effects. It is important to note that changes to your GC regimen may require changes to your mineralocorticoid regimen also. The study doctor will provide additional information if this is needed.

Throughout the course of the Glucocorticoid Conversion and Treatment periods, your GC dose may be adjusted from visit to visit, based on your test results and your symptoms. At each visit, your daily dose of GC will be either decreased, increased, or kept the same as before. As a person with CAH, you may already be familiar with some of the side effects or risks associated with changing your GC dose and taking too much or too little GC. Common symptoms associated with taking too much glucocorticoid may include, but are not limited to: increased body weight or fluid retention, changes in your mood (anxiety, depression, and other mood swings, etc.), changes in your appetite, and difficulty sleeping. Common symptoms associated with taking too little glucocorticoid may include, but are not limited to: fatigue, headaches, nausea, and abdominal pain. Overall, your CAH symptoms may improve, get worse, or stay the same as a result of the GC conversion and adjustments over the course of the study.

Please take note of any unwanted effects and report them to the study doctor immediately (if serious) or at your next visit.

Blood Draws

Blood samples that will be taken during the study will be always collected by qualified medical professional. Using a needle to remove blood from a vein is called a blood draw. It may be necessary to draw blood more than once. Possible side effects from drawing blood include faintness, inflammation of the vein, pain, bruising, or bleeding at the site puncture. There is also a slight possibility of infection. If you feel faint, you should tell the study doctor or study staff right away.

Fasting

Fasting could cause dizziness, headache, stomach discomfort, or fainting. If you feel faint, you should tell the study doctor right or study staff right away.

Ultrasound

Ultrasound is an imaging method to make pictures of organs inside your body. For males, you will lie on a table or a bed. A small amount of gel will be applied to your skin on the testes. A trained person will move a small probe over the testes, to capture images within the organ. An ultrasound takes about 30 minutes to complete. There are no known risks from a standard ultrasound.

DXA

During the scan you will lie on a padded table while a mechanical arm passes over your body to take x-rays of certain bones. You will need to hold very still, and you may even be instructed to hold your breath to prevent the image from being blurry. The DXA scan is painless. The amount of radiation you're exposed to is very low, less than between a few days and a few years of exposure to natural

radiation from the environment. Being exposed to X-rays does carry a risk of causing cancer many years or decades later, but this risk is thought to be very small.

Incidental Findings

As part of the study, it is the responsibility of the study doctor to tell you about any incidental findings. An incidental finding is a finding in a research participant discovered during a study, that is beyond the aims of the study, but which may have potential health importance. It is the responsibility of the study doctor to arrange for routine clinical review of study data and clinical follow-up as required.

You also have the right to not be informed about any incidental findings which may have potential health importance. Please indicate your decision (by signing your initials) below.

_____ Yes, I would like to be informed of any incidental findings.

_____ No, I would not like to be informed of any incidental findings.

Electrocardiogram (ECG)

For the ECG, 10 sticky patches connected by wires to a machine, will be placed on your chest, wrist and ankles. The ECG is painless and takes about 5 minutes. Skin irritation, such as redness or itching, is rare, but could occurring during the ECG from the electrodes or gel that is used.

Questionnaires

You will be asked to complete questionnaires about your CAH and quality of life. Completing the questionnaires could make you feel uncomfortable or upset. Some questions in the questionnaires may upset you. You should tell the study staff if you feel uncomfortable or upset while filling out a questionnaire. You have the right to refuse to answer any of the questions.

Pregnancy Risks

The effect of tildacerfont on an unborn baby, a breast-fed child, the female egg or on sperm is unknown. Therefore, you cannot participate in this study if you are pregnant, planning to become pregnant, are breastfeeding a child, or planning to father a baby during the study. If you are a female of child bearing potential (not post-menopausal or surgically sterilized), the study doctor must confirm you are not pregnant by performing a pregnancy test before you enter the study. Pregnancy tests will also be performed during the study to confirm that you did not become pregnant after entering the study. If you are a female of child bearing potential, you must use a highly effective contraceptive method and must not donate eggs while in the study and for at least 30 days after stopping the study drug.

If you become pregnant during the study, you will not be allowed to continue in the study and should call the study doctor right away. Your pregnancy will be followed until the completion of your pregnancy. Information about your pregnancy and its outcome will be collected and used to learn more about the effects of the study drug on pregnancy.

Acceptable methods of birth control include:

- Combined hormonal contraception (containing estrogen and progesterone): oral, intravaginal, or transdermal;
- Sexual partner with non-reversed vasectomy;
- Progesterone-only hormonal contraception associated with inhibition of ovulation: oral, injectable, or implantable intrauterine device or intrauterine system;
- Sexual abstinence, defined as refraining from heterosexual intercourse, if this is in line with your current lifestyle;
- Being post-menopausal as defined as no menses for at least 1 year;
- Documented hysterectomy or bilateral salpingectomy or oophorectomy.

If you are a male, you must not donate sperm while you are in the study and for at least 90 days after stopping the study drug. If you are a male and have a female partner who can become pregnant,

you must use an effective method of contraception (vasectomy, condom, true abstinence) while you are in the study and for at least 90 days after stopping the study drug. If you choose to use condoms for birth control, your female partner must use a highly effective method of contraception (described above) while you are in the study and for at least 90 days after you have stopped taking the study drug.

If your female partner becomes pregnant while you are participating in this study, or within 90 days after you have stopped taking the study drug, you should tell the study doctor promptly. If your partner provides consent, the Sponsor will collect information about the pregnancy and the outcome.

If applicable per country regulation, include the following language: If you agree to participate in this study, you are expected to inform your female sexual partner(s) that you are participating in a research study of a study medicine, and that the effects on sperm is unknown. You are also expected to provide your female sexual partner(s) with the information in the ***Pregnancy Risks*** section of this participant information and informed consent form, and to provide her with contact information for the study doctor for any additional questions.

New Information

Sometimes during the course of a research study, new information becomes available about the study drug. The study doctor will inform you in a timely manner about any new important information that is discovered during the study and discuss with you if you want to continue in the study. You may be asked to sign an updated participant information and informed consent form to confirm you agree to continue in the research study.

The study doctor may remove you from the study at any time without your consent. This may occur if:

- The study doctor does not consider it to be in your best interest to continue.
- You develop an illness that does not allow you to continue to receive the study treatment(s).
- You do not comply with the study requirements and are not able to follow the instruction from the study staff.
- You become pregnant.
- The study doctor has received new information about the safety or effectiveness of the study drug that would cause you to no longer be able to participate.
- You cannot tolerate the study drug.
- The study is stopped by the study site, the Sponsor, an IRB (Institutional Review Board)/EC (Ethics Committee), or a health authority.
- Certain laboratory (blood and urine) test results and heart monitoring test results may be cause for discontinuing the study if it is determined that the results are not safe.
- Responses to questionnaires that indicate you are at an increased risk for suicide or that you have become depressed or have increased anxiety.
- Changes to your adrenal hormone levels that are considered unsafe by the study doctor.

There may be other reasons based on the study doctor's judgement that are not listed here.

Benefits

You may or may not benefit as a result of your participation in this study. Results from this study may benefit others in the future.

Compensation for Injury

If you are injured because of your participation in this study, you should immediately notify the study doctor. The study doctor will recommend or provide medical treatment, including emergency treatment, if necessary. Your insurance may be billed for this treatment; however, you should check with your insurance company that taking part in this study will not affect your coverage under your medical insurance policy.

The study Sponsor will pay for the reasonable medical charges that are not covered by your insurance policy or other insurance programs available to you, and that are necessary to treat the

injury with the standard of care treatment, provided the injury was caused by the study drug or properly performed study procedures. You will not be reimbursed by the Sponsor for medical expenses related to the natural progression of, or failure of the study drug to improve, your disease, illness, or condition, any other pre-existing condition, or any injury or event that would have been expected from the standard treatment for your condition. You will not be reimbursed by the Sponsor for any injury that was caused by you or a third party.

Costs

The Sponsor, Spruce Biosciences, who has initiated the study is providing financial support and material for this study. *If applicable* The study site is being paid by Spruce Biosciences to do this study. Otherwise, the site staff including the study doctor have no financial ties to Spruce Biosciences.

There are no costs for you if you take part. You will receive the study drug free of charge and you will not be charged for any study-related procedures. You and your insurance company will have to pay for your daily GC dosing and any procedures unrelated to the study that are considered standard of care. Any additional costs for your GC dosing that are not covered by your insurance may be covered by the Sponsor. The study doctor can review these with you.

Because this is a research study, the study drug will be given to you only during this study and not after the study is over.

Compensation

The Sponsor is working with a third-party vendor to support travel, reimbursement (and visit stipend, if applicable) The third-party vendor will help ensure that the travel costs to attend study visits (fuel, bus, railway tickets, flight tickets, parking, hotels, food during travel/hotel stays, etc.) can be covered directly for you where possible to minimize your initial costs. In order to book travel (lyft/uber, flights, hotels, etc.) on your behalf for this study, the third-party vendor will need to use personally identifiable information (PII), such as your name, date of birth, address, email, and phone number. The third-party vendor will only use PII to schedule study related travel and not for any other purposes.

The third-party vendor can reimburse you directly by check, gift card, or wire transfer *(select according to the region/country, if applicable)* if you incur costs when travelling due to the study. In some cases, you may need to submit expenses and obtain reimbursement through your study center based on local site and IRB policies. The third-party vendor will need to collect the following information from you: full name, date of birth, address, email address, and phone number *include for EU only:* and bank account details.

For more details on what will be covered and how you will be reimbursed, or if you have questions, please refer to the material provided by the study doctor.

In situations where compensation is provided:
For your time and inconvenience related to your participation in this study, you will be paid for the study visits you complete according to the following schedule: [$xx.00] each for Visits [xx], [xx], and [xx]. If you do not complete the study, for any reason, you will be paid for each study visit you do complete according to the schedule above.

You will be reimbursed for your time when completing your eDiary at home. You may receive up to $850.00 United States Dollar (USD) or equivalent for completing your eDiary, depending on the number of eDiary entries you complete. This payment will be made by the third-party vendor, and the study staff can assist you with any questions regarding this payment.

If you agree to use the third-party vendor service, you will be asked to sign an additional informed consent form

If you do not want to use a third-party vendor service, you can get paid directly by the site.

OR

You will not receive any monetary compensation for your participation in this study.

Confidentiality

For EEA Countries
The study information will be collected by the study site and recorded in your medical records related to the study. Your personal data, which may be sensitive, including [day, month and year of birth, age, gender, race, ethnic origin] will be collected and handled electronically for the purpose of this study. Your study data will be handled in accordance with the European Union (EU) General Data Protection Regulation (GDPR) and other local regulations. You should ask the study doctor or a member of the study staff if you have questions about the results of your tests, other medical procedures, and confidentiality of your data.

The Sponsor, the Medpace group of companies (Medpace), representatives and contractors of the Sponsor or Medpace, regulatory authorities, Ethics Committees (ECs), and auditors may review your medical records and study data to check that the information that has been collected is correct and that the study has been carried out correctly. Your coded data may also be reviewed by the Sponsor, Medpace, representatives and contractors of the Sponsor or Medpace, the U.S. Food and Drug Administration (FDA), the European Medicines Agency (EMA), Ethics Committees (ECs), and other regulatory authorities in the U.S. and other countries evaluating the effects of the study drug for scientific research, on public health, and for a possible marketing authorization application. ECs are groups that look out for the rights and welfare of research participants.

Marken is a clinical supply chain organization that will be responsible for direct-to-patient shipping of the study drug to your home or place of work (or location that is convenient for you). DHL, or equivalent courier, may also be responsible for shipping the study drug from the site to your home. If you agree and if locally approved, the courier company (Marken, DHL, or other equivalent courier) will use your name, contact details (email, phone number), home address (or any other address you have provided as the delivery address) and other information that may be provided to perform the services (e.g., date of birth). To provide direct-to-patient services, Marken may also need to use your participant number or other similar information which is necessary for the delivery. Marken has security measures in place to safeguard your personal data, such as limiting access to personal data only to employees and authorized Service Providers. Marken will store your personal data to the extent necessary for the performance of Marken's obligations and strictly for the time necessary to achieve the purposes for which the data is kept. When your personal information is no longer needed, it will be removed from Marken's systems and records or Marken will take steps to remove participant identifiers from the data so you can no longer be identified from it.

Anyone who has access to this data will be bound to keep the information secure and confidential.

When you enter this study, you will be given a Participant Identification (SID) number. All data collected about you at the study site will be coded with this SID number. Your personal data, such as name and address, will be deleted and replaced with your SID number before any information leaves the study site. This way your data cannot be linked directly to you. The study doctor is responsible for keeping a code list, which makes it possible to link your SID number to your name. This will be kept in a safe place so you can be identified and contacted in case of emergency.

Your coded data may be transferred to the Medpace group of companies in the U.S. In some circumstances, your coded data may be transferred to other countries that do not have the same level of personal data protection as your country. If that occurs, the Sponsor and Medpace will take precautions to make sure your data is kept secure and confidential, and that your coded data will be transferred using adequate safeguards as required by GDPR.

You have the right to access and correct the information collected about you during this study as long as the study doctor keeps your medical information. You may also ask for and get a copy of your personal data and test results free of charge and have it sent to your regular doctor or specialist. *If applicable please add:* Your rights to access the information collected may be restricted until after completion of the study.

Your study data collected will be kept for a minimum of 25 years.

If you withdraw, no new data will be added to the study database. However, the study Sponsor may still use already collected information. If you decide to withdraw, you may also ask for identifiable samples to be destroyed to prevent further analysis.

The results of this study may be published, though you will not be identified in any report or publication. The study doctor will be given a copy of the report or publication at the end of the study.

A data controller is the party that controls the means and purposes of processing the data. The data processor is the party who processes the data for the data controller. In this study, the data controllers are [the study doctor and the Sponsor]; the data processor is Medpace. If you have any questions about your data, you should first contact the Data Protection Officer at the study site by e-mail. Please see contact information on the first page of this document. If you believe your data protection rights have been violated, you have the right to send a complaint to the [name of the Data Protection Authority of the country] by first contacting [the study doctor and/or the DPO of the study site or institution]. The legal basis under the GDPR for processing your personal data is a task carried out in the public interest in the area of public health and/or scientific purposes, and the legitimate interest of the Sponsor.

For U.S. only

Once this consent form is signed, you will be assigned a study code. During the study, the study doctor and study staff will collect your date of birth, gender, ethnicity, health data, and results of study procedures. Your study samples and records will not include your name or personal identity but will identify you with a study code. This code can only be tracked back to you via a code key which is held by the responsible physician. Although procedures are in place to protect your privacy, absolute confidentiality cannot be guaranteed.

Data will be stored, processed, and compiled by the Sponsor both manually and electronically. Your medical records and other personal information will be used and disclosed only in accordance with the law. Your identity will not be shared in any reports or publications resulting from this study. Your personal data, including health information, will be identified only by your study code when sent to Spruce Biosciences. This means that in most cases, your identification can be viewed only at the study site. Your medical records may be disclosed to and used by Spruce Biosciences, the Medpace group of companies (Medpace), representatives and contractors of the Sponsor or Medpace, the U.S. Food and Drug Administration (FDA), the European Medicines Agency (EMA), other agencies in the U.S. and other countries that have the right to review scientific research and medical records, Institutional Review Boards (IRBs), or any successors to any of these organizations. IRBs are groups that look out for the rights and welfare of research participants.

A description of this clinical trial will be available on http://www.ClinicalTrials.gov, as required by U.S. Law. This Web site will not include information that can identify you. At most, the Web site will include a summary of the results. You can search this Web site at any time.

A Federal law, called the Genetic Information Nondiscrimination Act (GINA), generally makes it illegal for health insurance companies, group health plans, and most employers to discriminate against you based on your genetic information. This law generally will protect you in the following ways:

- Health insurance companies and group health plans may not request your genetic information that we get from this research.
- Health insurance companies and group health plans may not use your genetic information when making decisions regarding your eligibility or premiums.
- Employers with 15 or more employees may not use your genetic information that we get from this research when making a decision to hire, promote, or fire you, or when setting the terms of your employment.

All health insurance companies and group health plans must follow this law as of May 21, 2010. All employers with 15 or more employees must follow this law as of November 21, 2009.

Be aware that this Federal law does not protect you against genetic discrimination by companies that sell life insurance, disability insurance, or long-term care insurance.

Marken is a clinical supply chain organization that will be responsible for direct-to-patient shipping of the study drug to your home or place of work (or location that is convenient for you). FedEx, or

equivalent courier, may also be responsible for shipping the study drug from the site to your home. If you agree and if locally approved, the courier company (Marken, FedEx, or other equivalent courier) will use your name, contact details (email, phone number), home address (or any other address you have provided as the delivery address) and other information that may be provided to perform the services (e.g., date of birth). To provide direct-to-patient services, Marken may also need to use your participant number or other similar information which is necessary for the delivery. Marken has security measures in place to safeguard your personal data, such as limiting access to personal data only to employees and authorized Service Providers. Marken will store your personal data to the extent necessary for the performance of Marken's obligations and strictly for the time necessary to achieve the purposes for which the data is kept. When your personal information is no longer needed, it will be removed from Marken's systems and records or Marken will take steps to remove participant identifiers from the data so you can no longer be identified from it.

Statement to be included in addition for E.E.A. countries:
A description of this trial will be available on https://euclinicaltrials.eu/search-for-clinical-trials as required by European countries laws *if applicable* [and also on [Local] website]. [This/these website(s)] will not include information that can identify you.

By signing and dating this consent form, you have not waived any of your legal rights, which you would have otherwise received, if you were not a participant in the study.

Whom to Contact About This Study

If you seek emergency care, or hospitalization is required, alert the treating physician that you are participating in this research study, show them your emergency contact card. If you have any questions or concerns about the research or your rights as a participant, an injury, or are unwell, please contact the study doctor or study staff. Please see contact details on the first page of this document.

All research studies are reviewed by an independent group of people called [Institutional Review Board (IRB)/Ethics Committee (EC)] to help protect the rights of research participants. This study has been reviewed and given [favorable opinion/approval] by [name of IRB/EC].

For studies conducted in the U.S. or countries where the EC/IRB can be contacted directly, add the following:
If you have any questions about your rights as a research participant, and/or concerns or complaints regarding this research study, you should write to [IRB/EC name and address], or call [IRB/EC phone number].

For E.E.A. Countries:

Participant Information and Informed Consent Form

Protocol Title:	A Randomized, Double-Blind, Placebo-Controlled Study to Evaluate the Efficacy and Safety of SPR001 (Tildacerfont) in Reducing Supraphysiologic Glucocorticoid Use in Adult Subjects with Classic Congenital Adrenal Hyperplasia
Protocol No.:	SPR001-204
EU CT No.:	2023-503771-13 [*for E.E.A. countries only*]
Sponsor:	Spruce Biosciences, Inc. 611 Gateway Blvd, Suite 740 South San Francisco, CA 94080 USA
Study Doctor:	[Insert Principal Investigator name and address]
24-hr. Telephone #:	[Insert 24-h phone number]
Data Protection Officer:	[Insert DPO name and e-mail address] **Sponsor's Data Protection Officer:** The DPO Centre 50 Liverpool Street London, EC2M 7PY, UK advice@dpocentre.com
	If Sponsor is located outside E.E.A.
Data Representative:	*[Insert data representative name and e-mail address if sponsor is outside EU] If it has been confirmed that Medpace will act as data representative add*: [Medpace Inc. e-mail: privacy@medpace.com]

- I have read and understand the information provided above.
- I confirm the study has been explained to me and that I have had the opportunity to ask questions and enough time to decide whether to participate. I know who to contact if I have further questions.
- I agree that biological samples (blood) collected from me can be stored and used for the purpose of this study.
- I agree that my (General Practitioner (GP)/personal physician) can be informed about my participation in this study.
- If I am unable to accommodate a clinic visit and am utilizing home health care, I authorize the licensed health care professionals, provided by the home health care provider, to have access to my personal data, including individually identifiable protected health information, such as name, address, and phone number as needed, to conduct the home care services for the study and to schedule home visits.
- I agree to take part in this study.

Participant's Printed Name

Participant's Signature Date

Consent for participants who cannot read

The study participant has indicated that he/she is unable to read. A member of the study staff has read the consent form to them and discussed it with them. The study participant has been given an opportunity to ask questions and all of his/her questions have been answered to his/her satisfaction.

Printed Name of Impartial Witness

Signature of Impartial Witness* Date

*Impartial Witness: A person, who is independent of the trial, who cannot be unfairly influenced by people involved with the trial, who attends the informed consent process if the participant or the participant's legally acceptable representative cannot read, and who reads the participant information and informed consent form and any other written information supplied to the participant. **Guidance for Industry E6 Good Clinical Practice: Consolidated Guidance**

Printed Name of the Person Obtaining Consent

Signature of the Person Obtaining Consent Date

For U.S. and non-E.E.A. countries:

Participant Information and Informed Consent Form

Protocol Title:	A Randomized, Double-Blind, Placebo-Controlled Study to Evaluate the Efficacy and Safety of SPR001 (Tildacerfont) in Reducing Supraphysiologic Glucocorticoid Use in Adult Subjects with Classic Congenital Adrenal Hyperplasia
Protocol No.:	SPR001-204
Sponsor:	Spruce Biosciences, Inc.
Study Doctor:	[Insert Principal Investigator name and address]
24-hr. Telephone #:	[Insert 24-h phone number]

I have read and understand the information in this participant information and informed consent form. I have had an opportunity to ask questions and all of my questions have been answered to my satisfaction. I voluntarily agree to participate in this study until I decide otherwise. I do not give up any of my legal rights by signing this participant information and informed consent form. I will receive a copy of this signed and dated participant information and informed consent form.

_____
Participant's Printed Name

_____ _____
Participant's Signature Date

Consent for participants who cannot read

The study participant has indicated that he/she is unable to read. A member of the study staff has read the consent form to them and discussed it with them. The study participant has been given an opportunity to ask questions and all of his/her questions have been answered to his/her satisfaction.

_____
Printed Name of Impartial Witness

_____ _____
Signature of Impartial Witness* Date

*Impartial Witness: A person, who is independent of the trial, who cannot be unfairly influenced by people involved with the trial, who attends the informed consent process if the participant or the participant's legally acceptable representative cannot read, and who reads the participant information and informed consent form and any other written information supplied to the participant. **Guidance for Industry E6 Good Clinical Practice: Consolidated Guidance**

_____
Printed Name of the Person Obtaining Consent

_____ _____
Signature of the Person Obtaining Consent Date

For U.S. only - should be deleted for all other countries

Authorization to Use and Disclose Protected Health Information

During your participation in this research study, the study doctor and study staff will collect or create personal health information about you (for example, medical histories and results of any lab tests, examinations, or procedures you undergo while in the study) and record it on study documents. The study doctor will keep this personal health information in your study-related records (that we will refer to as “your study records”). In addition, the study doctor may obtain, and include in your records, information regarding your past, present, and/or future physical or mental health and/or condition. The study doctor may ask you to sign a separate authorization to obtain some or all of your medical records from your regular doctor. Your study records may include other personal information (such as social security number, medical record numbers, date of birth, etc.), which could be used to identify you. Health information that could identify you is called “Protected Health Information” (or "PHI").

Under federal law (the “Privacy Rule”), your PHI that is created or obtained during this research study cannot be “used” to conduct the research or “disclosed” (given to anyone) for research purposes without your permission. This permission is called an “Authorization”. Therefore, you may not participate in this study unless you give your permission to use and disclose your PHI by signing this Authorization. By signing, you are agreeing to allow the study doctor and study staff to use and disclose your PHI to conduct this study.

By signing this Authorization, you also are agreeing to allow the study doctor to use and disclose your PHI as described below:

The Sponsor of this study and Medpace, and anyone working on behalf of the Sponsor and Medpace, including their contractors and representatives to conduct this study (referred to as “the Sponsor”), will analyze and evaluate your PHI and may use it to develop new tests, procedures, and commercial products. The study staff will assign a code number and/or letters to your study records, which means that you will not ordinarily be identified in the records sent to the Sponsor. The Sponsor may, however, look at your complete study records that identify you. In addition, the Sponsor may visit the study site to oversee the way the study is being conducted and may review your PHI during these visits to make sure the information is correct. The Institutional Review Board (“IRB”) may have access to your PHI in relation to its responsibilities as an Institutional Review Board.

The study doctor or Sponsor may disclose your PHI to the United States Food and Drug Administration (“FDA”) or similar regulatory agencies in the United States and/or foreign countries.

These disclosures also help ensure that the information related to this study is available to all parties who may need it for research purposes.

Except for the disclosures described above, your PHI will not be shared with others unless required by law. If your PHI is given to the parties listed above and/or to others who are not required to comply with the federal law, your PHI will no longer be protected by this law and could possibly be used or disclosed in ways other than those listed here.

You have a right to see and make copies of your PHI. If needed, you also have the right to correct any errors within your PHI. You are agreeing, however, by signing this Authorization, not to see or copy some or all of your PHI until the Sponsor has completed all work related to this study. At that time, you may ask to see your study records.

This Authorization does not have an expiration date from the date you sign it, unless you revoke (cancel or withdraw) it sooner.

You have a right to revoke your Authorization at any time. If you revoke it, your PHI will no longer be used for this study, except to the extent the parties to the research have already taken action based upon your Authorization, or need the information to complete analysis and reports for this research and to maintain the integrity or reliability of the current research. To revoke your Authorization, you must write to the study doctor, stating that you are revoking your Authorization to Use and Disclose Protected Health Information. Please see contact information on the first page of this document. If you revoke this Authorization, you will not be allowed to continue to be in this study.

You will receive a copy of this Authorization after you have signed and dated it.

_____
Printed Name of Participant

_____ _____
Signature of Participant Date

_____
Printed Name of the Person Obtaining the Authorization

_____ _____
Signature of the Person Obtaining the Authorization Date

FOR PARTICIPANTS WHO CANNOT READ

The study participant has indicated that he/she is unable to read. This Authorization document has been read to the participant by a member of the study staff, discussed with the participant by a member of the study staff, and the participant has been given an opportunity to ask questions of the study staff.

_____

Printed Name of Impartial Witness

_____ _____

Signature of Impartial Witness* Date

*Impartial Witness: A person, who is independent of the trial, who cannot be unfairly influenced by people involved with the trial, who attends the informed consent process if the participant or the participant's legally acceptable representative cannot read, and who reads the informed consent and any other written information supplied to the participant.

Guidance for Industry E6 Good Clinical Practice: Consolidated Guidance